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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/194,356	09/02/1999	DARIO NERI	515-4132	3100

23599 7590 12/29/2006  
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EXAMINER
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HARRIS, ALANA M

ART UNIT	PAPER NUMBER
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1643

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/29/2006	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

## Office Action Summary

**Application No.**

09/194,356

**Applicant(s)**

NERI ET AL.

**Examiner**

Alana M. Harris, Ph.D.

**Art Unit**

1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 05 October 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 30-47, 53-55 and 57-63 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 30-47, 53-55 and 57-63 is/are rejected.
- 7) ☒ Claim(s) 38-42 and 46 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>10/05/2006</u> . | 6) <input type="checkbox"/> Other: _____  |

**DETAILED ACTION**

***Response to Amendment and Arguments***

1. Claims 30-47, 53-55 and 57-63 are pending.  
Claims 62 and 63 have been added.  
Claim 46 has been amended.  
Claims 30-47, 53-55 and 57-63 are examined on the merits.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Withdrawn Grounds of Rejection***

***Claim Rejections - 35 USC § 112***

3. The rejection of claim 46 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of Applicants amendment to the claim.

***Maintained and New Grounds of Rejection***

***Claim Rejections - 35 USC § 102***

4. The rejection of claims 30-37, 43, 55, 57, 59, 60 and newly added claim 63 under 35 U.S.C. 102(b) as being anticipated by JP(A) H2-76598 (laid open March 15, 1990)/IDS reference number 23, submitted February 8, 2005 is maintained and made.

Applicants have provided a 1.132 declaration by the main inventor, Dr. Sekiguchi providing assertions, as well as experiments, which purportedly teach away from the prior art. The declaration and corresponding arguments, particularly 3<sup>rd</sup> paragraph on page 6 of the Remarks submitted October 5, 2006 over the antibodies prepared in the Japanese application are not specific for an epitope in the ED-B domain of fibronectin. Applicants reference page 9, lines 24-31 but do not indicate what document one should review. If indeed Applicants are referencing their own patent application this section of the application defines, specific and does not aid in clarifying the instant issues.

The Examiner has carefully reviewed the declaration and its information therein. This information and particular the experiments therein have been thoroughly assessed and found to be insufficient and unpersuasive. Dr. Sekiguchi presents an experiment that supposedly demonstrates lack of binding of the CF525 antibody, also known as OAL-CF525 to the ED-B domain of fibronectin. This assertion and the experiment is confusing because JP(A) H2-76598 clearly discloses a monoclonal antibody, which specifically recognizes the ED-B domain comprising 91 amino acids, see page 2, first and third paragraph. These amino acids are the same as the ED-B domain of Applicants. It is not clear how the implementation of antigen fragments of the ED-B peptide for the manufacture of antibodies would yield antibodies that are contravene to those the Japanese patent asserts were manufactured and read on the claimed invention, see pages 11, 13 and 14, Manufacturing...sections. And while Dr. Sekiguchi's declaration presents data, this information does not preclude the binding of the anticipatory antibodies to the ED-B oncofoetal domain of FN, especially in light of

Art Unit: 1643

the conclusion sentence. This sentence notes "[t]he antibodies of my Japanese patent application H2-76598 and H4-169195 *do not seem* to be specific for the ED-B domain of fibronectin.", see page 6, paragraph 9. It is requested Applicants clearly establish why and how the prior art antibodies do not definitively bind directly to the ED-B oncofoetal domain of FN as expressed in the prior art. For the reasons of record and the analysis provided above the rejection is maintained.

8. The rejection of claims 30-37, 43, 47, 55, 57, 59-61 and newly added claim 63 under 35 U.S.C. 102(b) as being anticipated by JP(A) H4-169195 (laid open June 17, 1992)/ IDS reference number 24, submitted February 8, 2005 is maintained and made. Applicants' arguments directed toward this 102(b) rejection are similarly presented as that set forth in the initial 102(b) rejection.

The Examiner's position for this rejection is the same for the first cited 102(b) rejection and the rejection is maintained for the reasons of record. The Examiner has carefully reviewed the declaration and its information therein. This information and particular the experiments therein have been thoroughly assessed and found to be insufficient and unpersuasive. Dr. Sekiguchi presents an experiment that supposedly demonstrates lack of binding of the TFN-01 antibody, also known as OAL-TFN-01 to the ED-B domain of fibronectin, see page 4 of the Declaration. This assertion and the experiment is confusing because JP(A) H4-169195 not only discloses this antibody, but other antibodies, see page 18, last sentence and page 2, 3<sup>rd</sup> full paragraph. It is not clear how the implementation of antigen fragments of the ED-B peptide for the

Art Unit: 1643

manufacture of antibodies would yield antibodies that are contravene to those the Japanese patent asserts were manufactured and read on the claimed invention, see pages 11, 13 and 14, Manufacturing...sections. And while Dr. Sekiguchi's declaration presents data, this information does not preclude the binding of the anticipatory antibodies to the ED-B oncofoetal domain of FN, especially in light of the conclusion sentence. This sentence notes "[t]he antibodies of my Japanese patent application H2-76598 and H4-169195 *do not seem* to be specific for the ED-B domain of fibronectin.", see page 6, paragraph 9. It is requested Applicants clearly establish why and how the prior art antibodies do not definitively bind directly to the ED-B oncofoetal domain of FN. For the reasons of record and the analysis provided above the rejection is maintained.

9. The rejection of claims 30-32, 34-37, 43, 47, 53, 55, 57-61 and newly added claims 62 and 63 under 35 U.S.C. 102(b) as being anticipated by U.S. Patent number 4,894,326 (issued January 16, 1990/ IDS reference 1, submitted August 15, 2005) is maintained and made.

Applicants argue the passages cited by the Examiner and Masuura "...hints that FDC-6 is not specific for the ED-B domain" are reasons to withdraw the instant rejection, see page 6, last paragraph of Applicants' Remarks. Applicants direct the Examiner's attention to Figure 2A of patent '326 noting it shows the location of the ED-B domain. Moreover, Applicants assert the Matsuura reference of 1988 confirms "...the FDC-6 antibody defines a structure, not at the ED-B domain" and an attached five page PowerPoint illustration of fibronectin structures further clarifies this assertion. These

Art Unit: 1643

points of view and the submitted articles have been carefully considered, but found unpersuasive.

Foremost, the reference PowerPoint illustration did not accompany the October 5<sup>th</sup> submission and the Matsuura reference does not teach away from the disclosure presented in the patent.

U.S. Patent 4,894,326 discloses an IgG1 monoclonal antibody (FDC-6), which defines the oncofoetal structure within fibronectin, see column 2, lines 41-47 and 60-63; and column 3, lines 2-8. The patent discloses the FDC-6 and other immunological binding partners such as antigen-binding fragments and chimearas comprised in a suitable carrier and introduced into the body of a mammal, see bridging paragraph of columns 4 and 5. "The FDC-6 antibody, as well as other antibodies raised against the oncofoetal structure, can be packaged in kits useful for assaying the presence of oncofoetal fibronectin", see column 5, lines 39-44. Inherently, the disclosed antibody has all the properties as deemed by the antibody or antibody fragment, which binds directly to an ED-B oncofoetal domain of fibronectin (FN) and the rejection is maintained.

### ***Claim Rejections - 35 USC § 103***

10. The rejection of claims 30-37, 43-45, 55, 57-60 and newly added claims 62 and 63 under 35 U.S.C. 103(a) as being unpatentable over JP(A) H2-76598 (laid open March 15, 1990)/ IDS reference number 23, submitted February 8, 2005, in view of Bird et al. (Science 242:423-242, 1988) is maintained for the reasons of record.

Art Unit: 1643

11. The rejection of claims 30-37, 43-45, 47, 55, 57-61 and newly added claims 62 and 63 under 35 U.S.C. 103(a) as being unpatentable over JP(A) H4-169195 (laid open June 17, 1992)/ IDS reference number 24, submitted February 8, 2005, in view of Bird et al. (Science 242:423-242, 1988) is maintained for the reasons of record.

12. The rejection of claims 30-37, 43, 47, 53-57, 59, 60 and newly added claims 62 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP(A) H2-76598 (laid open March 15, 1990)/ IDS reference number 23, submitted February 8, 2005, in view of Clackson et al. (Nature 352:624-628, August 15, 1991) is maintained for the reasons of record.

13. The rejection of claims 30-37, 43, 47, 54, 55, 57, 59-61 and newly added claims 62 and 63 under 35 U.S.C. 103(a) as being unpatentable over JP(A) H4-169195 (laid open June 17, 1992)/ IDS reference number 24, submitted February 8, 2005, in view of Clackson et al. (Nature 352:624-628, August 15, 1991) is maintained for the reasons of record.

14. The rejection of claims 30-37, 43, 53, 55, 57, 59, 60 and newly added claims 62 and 63 under 35 U.S.C. 103(a) as being unpatentable by JP(A) H2-76598 (laid open March 15, 1990)/ IDS reference number 23, submitted February 8, 2005 is maintained for the reasons of record.

15. The rejection of claims 30-37, 43, 53, 55, 57, 59, 60 and newly added claims 62



Art Unit: 1643

and 63 under 35 U.S.C. 103(a) as being unpatentable by JP(A) H2-76598 (laid open March 15, 1990)/ IDS reference number 23, submitted February 8, 2005 is maintained for the reasons of record.

16. The rejection of claims 30-32, 34-37, 43-45, 47, 53, 55, 57-61 and newly added claims 62 and 63 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 4,894,326 (issued January 16, 1990/ IDS reference 1, submitted August 15, 2005), and further in view of in view of Bird et al. (Science 242:423-242, 1988) and Clackson et al. (Nature 352:624-628, August 15, 1991) is maintained for the reasons of record.

***Allowable Subject Matter***

17. Claims 38-42 and 46 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Conclusion***

18. Claims 38-42 and 46 are free of the art.

19. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Art Unit: 1643

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571) 272-0831. The Examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm, with alternate Fridays off.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1643

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

**ALANA M. HARRIS, PH.D.**

**PRIMARY EXAMINER**



Alana M. Harris, Ph.D.

19 December 2006